510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY

A. 510(k) Number:

K121100

B. Purpose for Submission:

The addition of Vancomycin to the Vitek 2 and Vitek 2 Compact Antimicrobial Susceptibility Test (AST) Systems for Streptococcus spp. (*S. agalactiae, S. pyogenes* and Viridans Group *Streptococci)*

C. Measurand:

Vancomycin ≤ 0.125 – 8 μg/mL

D. Type of Test:

Determination of the minimum inhibitory concentration (MIC) determined using a quantitative growth based algorithm with a predetermined growth threshold.

E. Applicant:

bioMerieux, Inc.

F. Proprietary and Established Names:

Vitek® 2 AST Streptococcus Vancomycin

G. Regulatory Information:

1. Regulation section:

   21 CFR 866.1645 – Short-Term Antimicrobial Susceptibility Test System

2. Classification:

   Class II

3. Product code:
   LON – System, Test, Automated, Antimicrobial Susceptibility, Short Incubation

4. Panel:

83 Microbiology

H. Intended Use:

1. Intended use(s):

VITEK® 2 AST *Streptococcus* Vancomycin is designed for antimicrobial susceptibility testing of Streptococcus species. VITEK® 2 AST Streptococcus Vancomycin is a quantitative test intended for use with the VITEK® 2 and VITEK® 2 Compact Systems as a laboratory aid in the determination of in vitro susceptibility to antimicrobial agents. Vancomycin has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antimicrobial.

Active *in vitro* and in clinical infections
Viridans group streptococci

In vitro data are available, but their clinical significance is unknown
Streptococcus agalactiae
Streptococcus pyogenes

The VITEK® 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK® 2 System for the automated quantitative or qualitative susceptibility testing of isolated colonies for the most clinically significant aerobic gram-negative bacilli, *Staphylococcus spp., Enterococcus spp., Streptococcus spp.* and clinically significant yeast.

2. Indication(s) for use:

VITEK® 2 AST *Streptococcus* Vancomycin is designed for antimicrobial susceptibility testing of Streptococcus species. VITEK® 2 AST Streptococcus Vancomycin is a quantitative test intended for use with the VITEK® 2 and VITEK® 2 Compact Systems as a laboratory aid in the determination of in vitro susceptibility to antimicrobial agents. Vancomycin has been shown to be active against most strains of the microorganisms listed below, according to the FDA label for this antimicrobial.

Active *in vitro* and in clinical infections
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In vitro data are available, but their clinical significance is unknown
Streptococcus agalactiae
Streptococcus pyogenes

The VITEK® 2 Antimicrobial Susceptibility Test (AST) is intended to be used with the VITEK® 2 System for the automated quantitative or qualitative

susceptibility testing of isolated colonies for the most clinically significant aerobic gram-negative bacilli, *Staphylococcus spp., Enterococcus spp., Streptococcus spp.* and clinically significant yeast.

3. Special conditions for use statement(s):

   For prescription use only.

4. Special instrument requirements:

   For use with VITEK® 2 and VITEK® 2 Compact Systems

I. Device Description:

The VITEK® 2 AST card is a miniaturized, abbreviated and automated version of the doubling dilution technique for determining the minimum inhibitory concentration (MIC). Each VITEK® 2 AST card contains 64 micro wells. A control well, which contains only microbiological culture media, is present on all cards. The remaining wells contain premeasured portions of specific antibiotics in a culture media base. The bacterial isolate to be tested is diluted to a standardized concentration with 0.45-0.5% saline before being used to rehydrate the antimicrobial medium in the wells in the card. The VITEK® 2 System automatically fills seals and places the card into the incubator/reader. With VITEK® 2 Compact the filling, sealing and loading of the card is done manually. The VITEK® 2 Systems monitor the growth of each well in the card over a defined period of time. At the completion of the incubation cycle, a report is generated which includes the MIC value and the result interpretation for each antibiotic.

The VITEK® 2 AST *Streptococcus* Vancomycin has the following concentrations in the card: 0.5, 1, 2, and 4 µg/mL (equivalent standard method concentration by efficacy in µg/mL). The MIC result range for the VITEK® 2 cared is 0.125 – 8 µg/mL.

Vitek® 2 AST-ST	Equivalent Standard Method Conc. By Efficacy in µg/mL	MIC Ranges and CLSI/FDA Categories (MIC in µg/mL)		
		S**	I	R
Vancomycin	0.5, 1, 2, 4	≤1†Ψ	-	-

** Currently only a "Susceptible" category is defined for vancomycin. Isolates yielding results suggestive of "nonsusceptible" should be submitted to a reference laboratory for further testing.

† Interpretative criteria is applicable only to tests performed by broth microdilution method using cation-adjusted Mueller-Hinton broth with 2 to 5% lysed horse blood.

ΨThe FDA approved drug label designates this interpretive criteria only for "Streptococci other than *S. pneumoniae"*.

J. Substantial Equivalence Information:

1. Predicate device name(s):

   VITEK® 2 Gram Positive Amoxicillin for *Streptococcus pneumoniae*

2. Predicate K number(s):

   K063597

3. Comparison with predicate:

Similarities		
Item	Device	Predicate
1. Intended Use	Determine antimicrobial susceptibility to antimicrobial agents	Same
2. Inoculum	Saline suspension of organism	Same
3. Instrument	Vitek 2 System	Same
4. Test Card	Vitek 2 Test Card	Same

Differences		
Item	Device	Predicate
1. Antimicrobial Agent	Vancomycin with specific drug concentrations	Amoxicillin with specific drug concentrations
2. Isolates	Viridans Group Streptococcus, *S. agalactiae*, *S. pyogenes*	*S. pneumoniae*
3. Reading Algorithm	Unique for Vancomycin	Unique for Amoxicillin

K. Standards/Guidance Documents referenced (if applicable):

1. Class II Special Controls Guidance Document: Antimicrobial Susceptibility Test Systems; Guidance for Industry and FDA; August 28, 2009
2. CLSI M100-S19: Performance Standards for Antimicrobial Susceptibility Testing; Nineteenth Informational Supplement.
3. CLSI M07-A8: Methods for Dilution Antimicrobial Susceptibility Tests for Bacteria That Grow Aerobically; Approved Standard.-Eighth edition.

L. Test Principle:

The VITEK® 2 System optics use visible light to directly measure organism growth. These transmittance optics are based on an initial light reading of a well before significant growth has begun. Periodic light transmittance samplings of the same well measure organism growth by how much light is prevented from going through the well. An interpretive call is made between 4 and 16 hours for a "rapid" read by may be extended to 18 hours in some instances. The VITEK® 2 Susceptibility Card test is based on the microdilution minimum inhibitory concentration technique with concentrations equivalent to standard method concentrations. Several parameters based on the growth characteristics observed are used to provide appropriate input for the MIC calculations. Discriminate analysis is used to develop the algorithm that determines the susceptibility result for all antimicrobials on the VITEK® 2 System. The MIC result must be linked to organism identification in order to determine a category interpretation. A category

interpretation (SIR) will be reported along with an MIC.

M. Performance Characteristics (if/when applicable):

1. Analytical performance:

   a. *Precision/Reproducibility:*

   Reproducibility testing was performed using 10 Streptococcal isolates at 3 study sites on 3 separate days, in triplicate. The study included both the auto-dilution and manual dilution methods with the VITEK® 2 and the manual dilution method with the VITEK® 2 Compact. All results were >95% reproducible.

   b. *Linearity/assay reportable range:*

   Not Applicable

   c. *Traceability, Stability, Expected values (controls, calibrators, or methods):*

   The recommended quality control isolate, namely, *S. pneumoniae* ATCC 49619, was tested on every test occasion with the reference method and the VITEK® 2, using both auto- and manual dilution methods.
   All results fell within acceptable range which demonstrates that the VITEK® 2 can consistently produce quality control results in the recommended range for Vancomycin.

QC Table - VITEK®2 (Auto- and Manual Dilution Method)

ORGANISM	Conc. (µg/mL)	Vitek 2 Auto-dilution		Vitek 2 Manual dilution	
		Test	Ref.	Test	Ref.
S. pneumoniae ATCC 49619 **Expected Range : 0.12-0.5 µg/mL**	0.0625				
	0.125*	8	2	10	2
	0.25	206	209	205	210
	0.5		3		3

*** This value is indicated as ≤ 0.125 for the VITEK® 2 System.**

An additional quality control study was conducted with the VITEK® 2 Compact, the secondary option. Testing took place at 3 study sites, with the following results.

QC Table - VITEK®2 Compact (Manual Dilution Method)

ORGANISM	Conc. (µg/mL)	Manual dilution	
		Test	Ref.
S. pneumoniae ATCC 49619 **Expected Range : 0.12-0.5µg/mL**	0.0625		
	0.125		
	0.25	60	57
	0.5		3

The DensiCHEK™ was used at each site to standardize the inoculum for the VITEK® 2 AST cards. Calibration of the DensiCHEK™ was performed weekly. All results were recorded and fell within acceptable range.

d. Detection limit:

Not Applicable

e. Analytical specificity:

Not Applicable

f. Assay cut-off:

Not Applicable

2. Comparison studies:

a. Method comparison with predicate device:

Clinical study testing was conducted at four external sites using the VITEK®2 Streptococcus Vancomycin AST card and the broth microdilution reference method using Mueller-Hinton broth with lysed horse blood prepared as recommended by the CLSI. Performance testing included a total of 1099 clinical isolates, both fresh and stock (13.6%). Testing of the clinical isolates was performed using the automated method of inoculation. Performance data comparing the VITEK®2 Streptococcus Vancomycin and the reference method is illustrated in Table A below.

Challenge study testing was conducted, at one external site using the VITEK® 2 *Streptococcus* Vancomycin AST card and the broth microdilution reference method using Mueller-Hinton broth with lysed horse blood prepared as recommended by the CLSI. A challenge set consisting of a total of 150 isolates, including 50 isolates of *S. agalactiae,* 50 isolates of *S. pyogenes* and 50 isolates of *Viridans Group Streptococcus* was used for the performance testing. Testing of the challenge isolates was performed using both auto-dilution and manual dilution method. As is illustrated in Tables A and B below, there is very little difference in the device performance between the two types of dilution methods.

Challenge testing of the VITEK®2 Streptococcus Vancomycin AST card in combination with the VITEK®2 COMPACT instrument was also conducted against the broth microdilution reference method, at one external site, using the same challenge set of 150 isolates. Testing was performed using the manual dilution method. The performance data is illustrated in Table C below.

Table A. VITEK2/ Streptococcus Vancomycin Auto-dilution	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Clinical	1099	1049	95.5	1077	1044	96.9	1099	100	0	0	0	0
Challenge	150	148	98.7	149	148	99.3	150	100	0	0	0	0
Combined	1249	1197	95.8	1226	1192	97.2	1249	100	0	0	0	0

Table B. VITEK2/ Streptococcus Vancomycin Manual Dilution	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Challenge	150	148	98.7	149	148	99.3	150	100	0	0	0	0

Table C. VITEK 2 Compact/ Streptococcus Vancomycin Manual Dilution	Tot	EA N	%EA Total	Total Eval	EA Eval	%EA Eval	CA N	%CA	#R	min	maj	vmj
Challenge	150	149	99.3	149	149	100	150	100	0	0	0	0

EA = Essential Agreement
CA = Category Agreement
R = Resistant Isolates
min = minor discrepancies
maj = major discrepancies
vmj = very major discrepancies

Evaluable results are those that fall within the test range of the reference method and could also be on-scale with the new device if within plus/minus one dilution. Essential Agreement (EA) occurs when there is agreement between the result of the reference method and that of VITEK® within plus or minus one serial two-

fold dilution of the antibiotic. Category Agreement (CA) occurs when the interpretation of the result of the reference method agrees exactly with the interpretation of the VITEK® result.

Relative to all the clinical and challenge testing performed using the VITEK®2 *Streptococcus* Vancomycin, the overall %EA and %CA consistently met the acceptance criteria of greater than or equal to 90%. There were no categorical errors.

Relative to all the clinical and challenge testing performed using the VITEK®2 *Streptococcus* Vancomycin test card, there were no instances of growth failure.

b. Matrix comparison:

Not Applicable

3. Clinical studies:

a. Clinical Sensitivity:

Not Applicable

b. Clinical specificity:

Not Applicable

c. Other clinical supportive data (when a. and b. are not applicable):

Not applicable

4. Clinical cut-off:

Not applicable

5. Expected values/Reference range:

According to the most up to date FDA drug label the interpretive criterion for Vancomycin for Streptococcal isolates other than *S. pneumoniae* is : <1 (S)

N. Proposed Labeling:

The labeling is sufficient and satisfies the requirements for 21 CFR section 809.10.

O. Conclusion:

The submitted information in this premarket notification is complete and supports a substantial equivalence decision.